

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : 6,899,915 B2  
APPLICATION NO. : 09/997734  
DATED : May 31, 2005  
INVENTOR(S) : Dunn

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It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

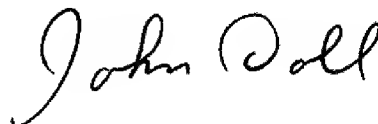
Delete Title page illustrating figure, and substitute new Title page illustrating figure attached.

Delete drawing sheets 1-20, and substitute drawing sheets 1-20, with the attached sheets.

This certificate supersedes the Certificates of Correction issued August 8, 2006 and June 30, 2009.

Signed and Sealed this

Fourth Day of August, 2009

A handwritten signature in black ink that reads "John Doll". The signature is written in a cursive, flowing style.

JOHN DOLL  
*Acting Director of the United States Patent and Trademark Office*

(12) **United States Patent**  
Yelick et al.

(10) **Patent No.:** **US 6,899,915 B2**  
(45) **Date of Patent:** **May 31, 2005**

(54) **METHODS AND COMPOSITIONS FOR CULTURING A BIOLOGICAL TOOTH**

(75) **Inventors:** Pamela C. Yelick, Concord, MA (US); John D. Bartlett, Acton, MA (US); Joseph P. Vacanti, Winchester, MA (US); Bjorn R. Olsen, Milton, MA (US); Phillip Stashenko, Medfield, MA (US)

(73) **Assignees:** President and Fellows of Harvard College, Cambridge, MA (US); General Hospital Corporation, Boston, MA (US); Forsyth Dental Infirmary for Children, Inc., Boston, MA (US)

(\*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) **Appl. No.:** 09/997,734

(22) **Filed:** Nov. 29, 2001

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**Related U.S. Application Data**

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(51) **Int. Cl.<sup>7</sup>** ..... A61C 13/08

(52) **U.S. Cl.** ..... 427/2.26; 433/302.1; 433/204; 264/19; 523/115

(58) **Field of Search** ..... 427/2.26, 2.27, 433/202.1, 204, 215, 223; 264/19; 523/115, 521/50, 51, 55; 514/21; 424/435; 623/23.58, 23.72, 23.75

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*Primary Examiner*—James J. Seidleck

*Assistant Examiner*—Melanie Bissett

(74) *Attorney, Agent, or Firm*—Banner & Witcoff, Ltd.

(57) **ABSTRACT**

Tooth tissues include the pulp mesenchyme that forms the dentin and an epithelium that is responsible for enamel formation. Cells from these tissues were obtained from porcine third molars and were seeded onto a biodegradable scaffold composed of a polyglycolic acid—polylactic acid copolymer. Cell polymer constructs were then surgically implanted into the ormentum of athymic nude rats so that the constructs would have a blood supply and these tissues were allowed to develop inside the rats. Infrequently, columnar epithelial cells were observed as a single layer on the outside of the dentin-like matrix similar to the actual arrangement of ameloblasts over dentin during early tooth development. Developing tooth tissues derived from such cell polymer constructs could eventually be surgically implanted into the gum of an edentulous recipient where the construct would receive a blood supply and develop to maturity, providing the recipient with a biological tooth replacement.

**54 Claims, 20 Drawing Sheets**



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Tooth Scaffolds

PGA + PLLA



Fig. 1

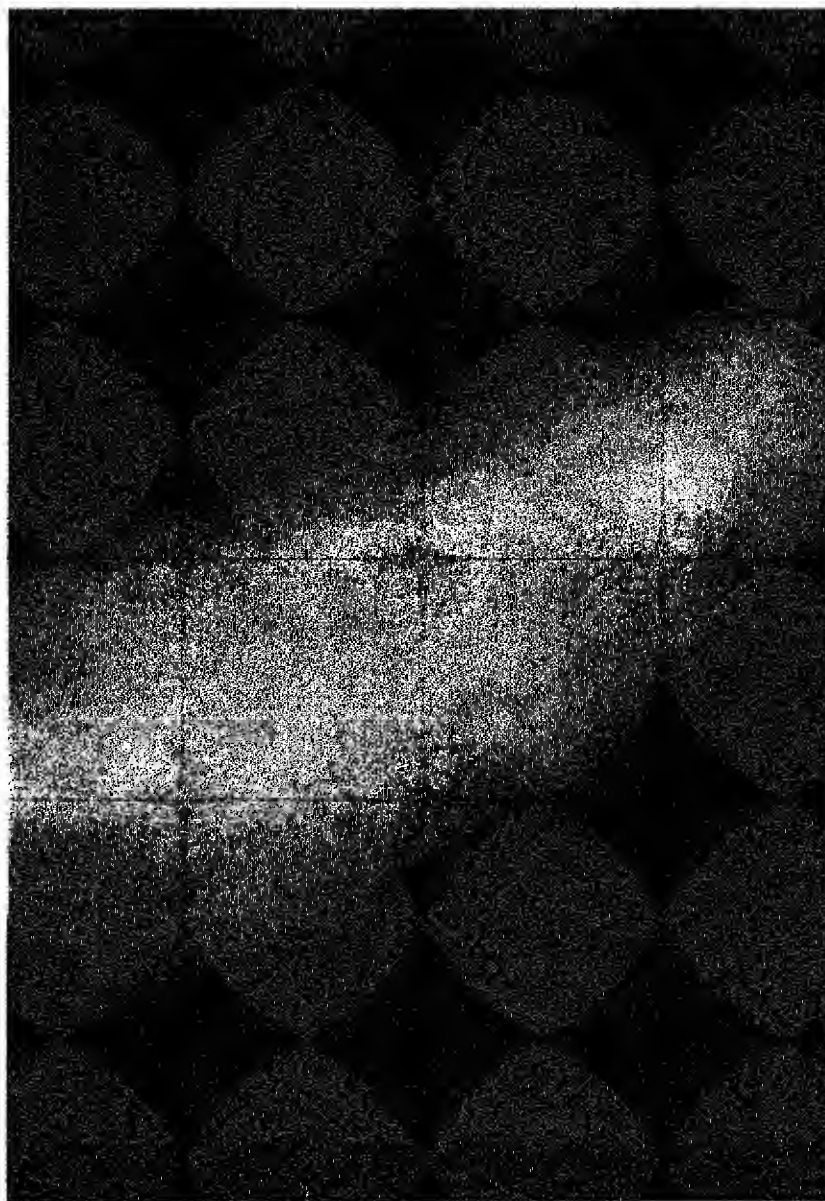
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Tooth Scaffolds-PLGA



**Fig. 2**

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SEM-PLGA Scaffold + Salt

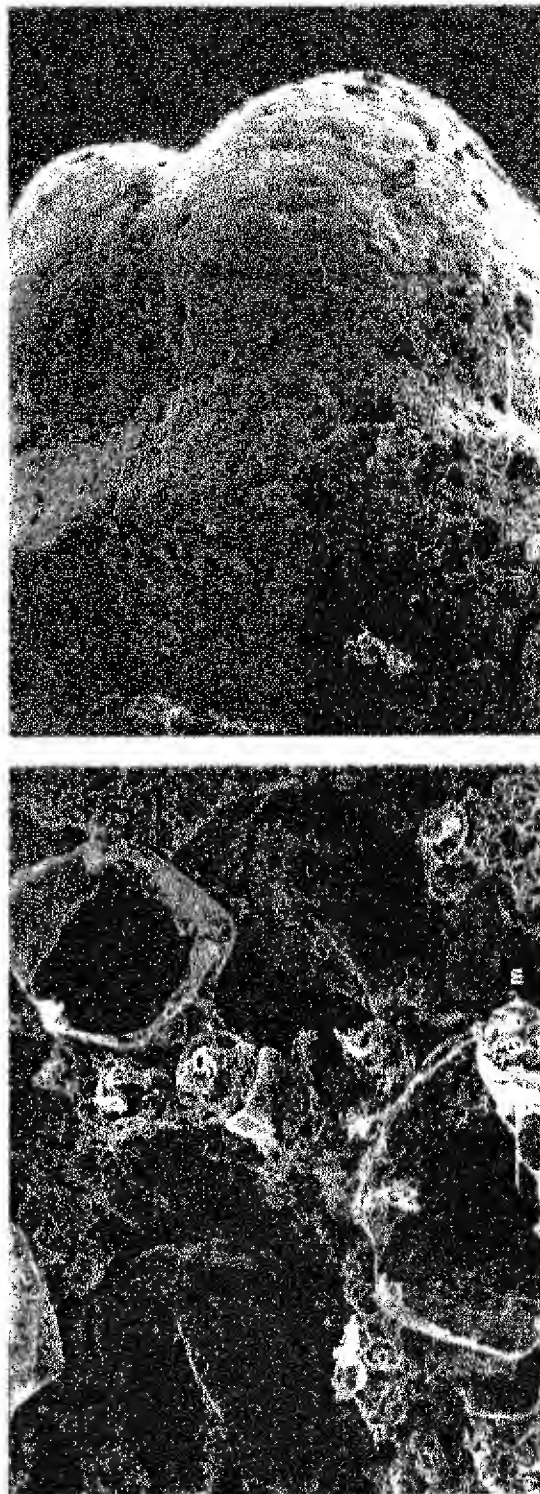


Fig. 3

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SEM-PLGA Scaffold + Sugar

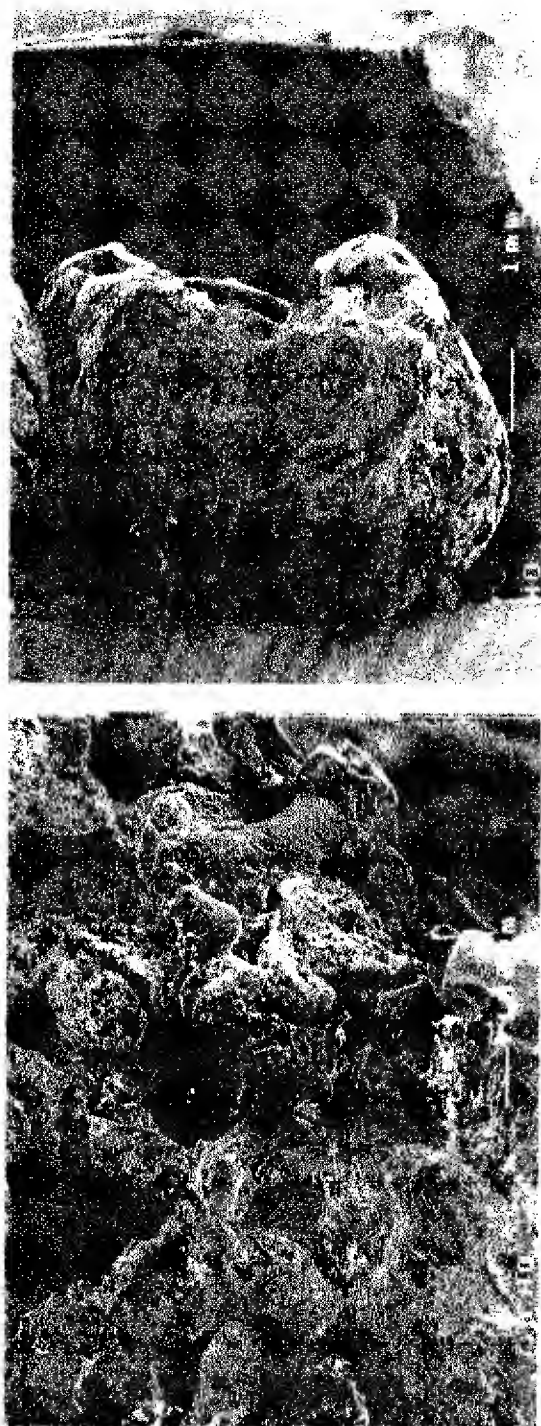


Fig. 4

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**Removal of Porcine Third Molar**



**Fig. 5**



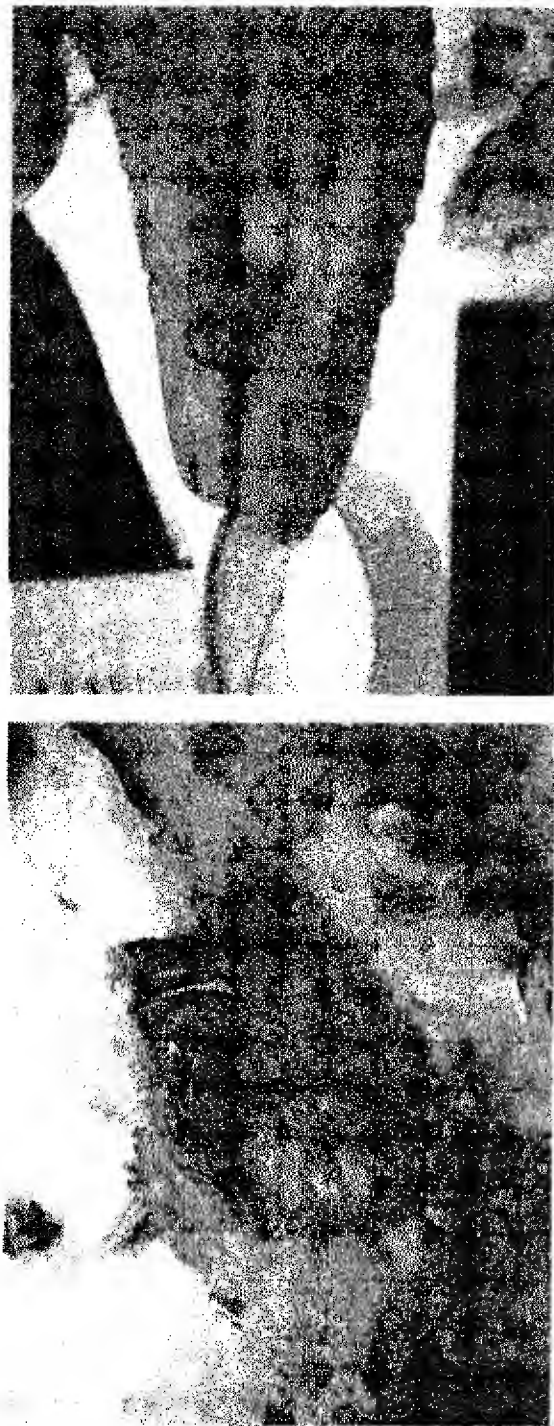
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Removal of Porcine Third Molar



**Fig. 6**



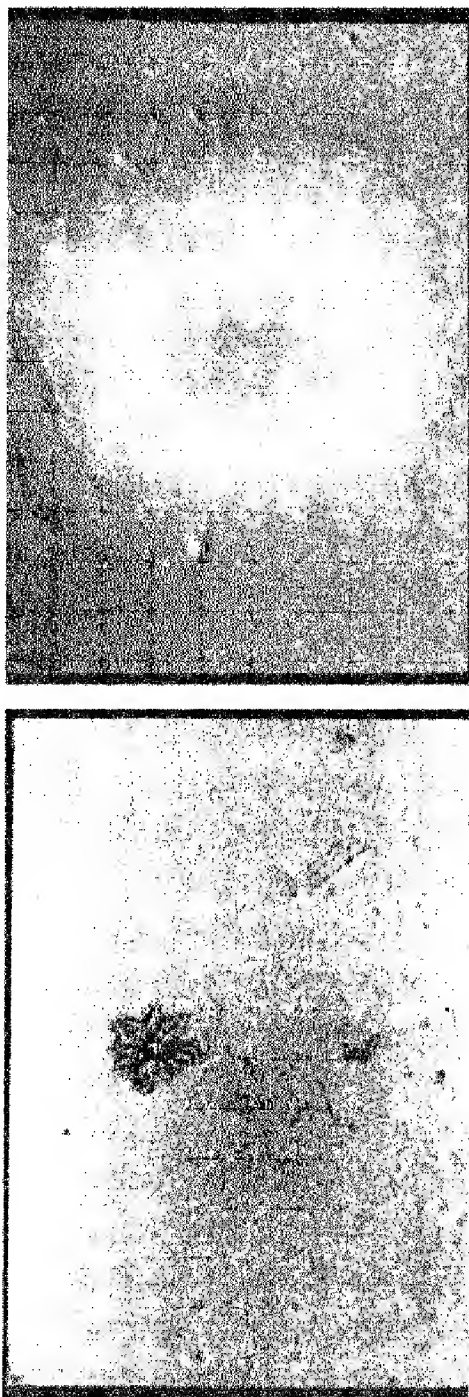
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Porcine Tooth Tissue Culture



**Fig. 7**

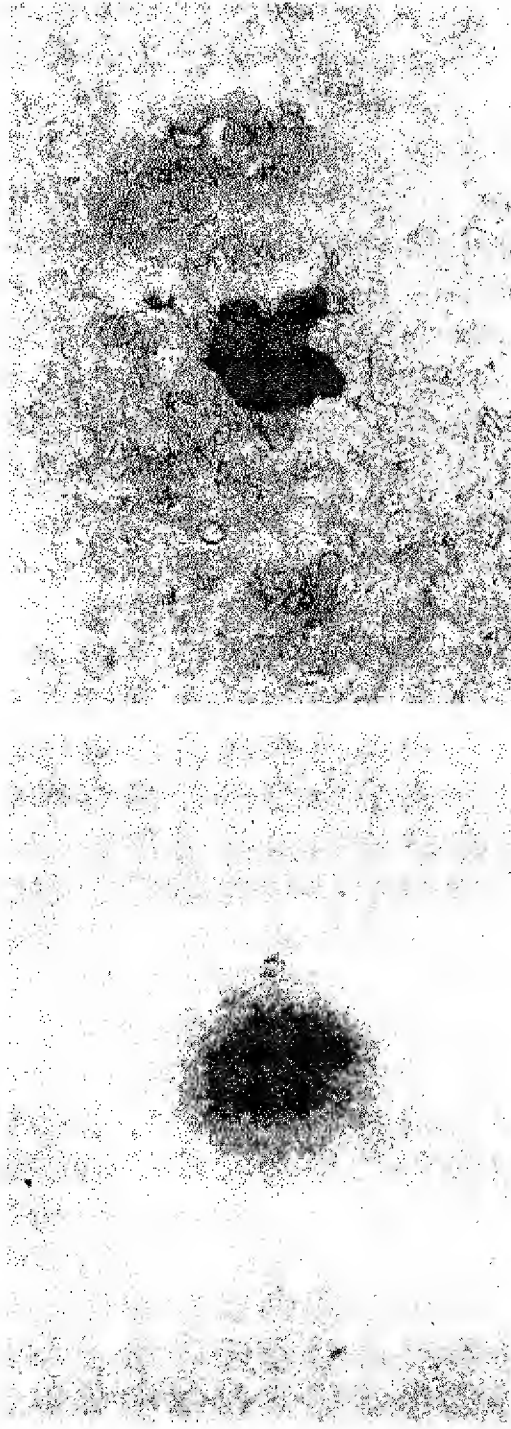
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**Tissue Culture-Von Kossa Stain**



**Fig. 8**

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Rat Radiographs - Human Tooth



**Fig. 9**

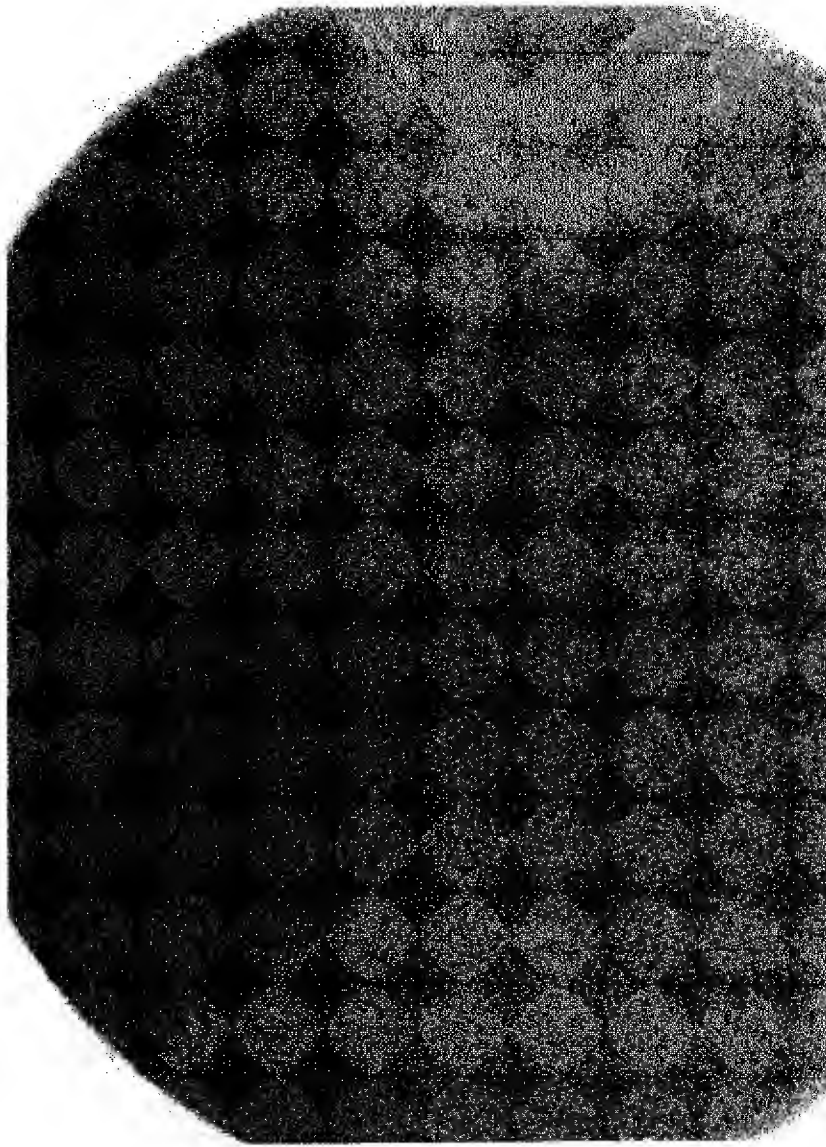
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**Rat Radiographs - Implant, 7.5 weeks**



**Fig. 10**

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Dissection of Tissue



**Fig. 11**

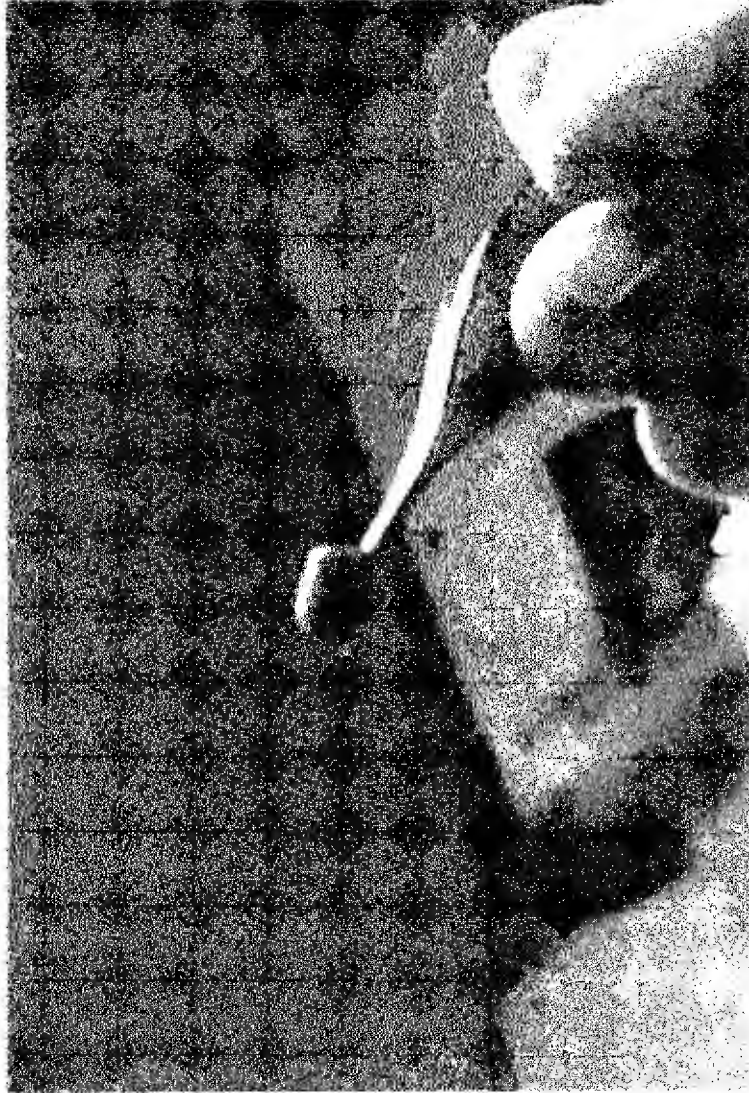
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Dissection of Tooth Tissue  
7.5 weeks



**Fig. 12**



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**Dissected Tooth Tissue - 7.5 Weeks**



**Fig. 13**



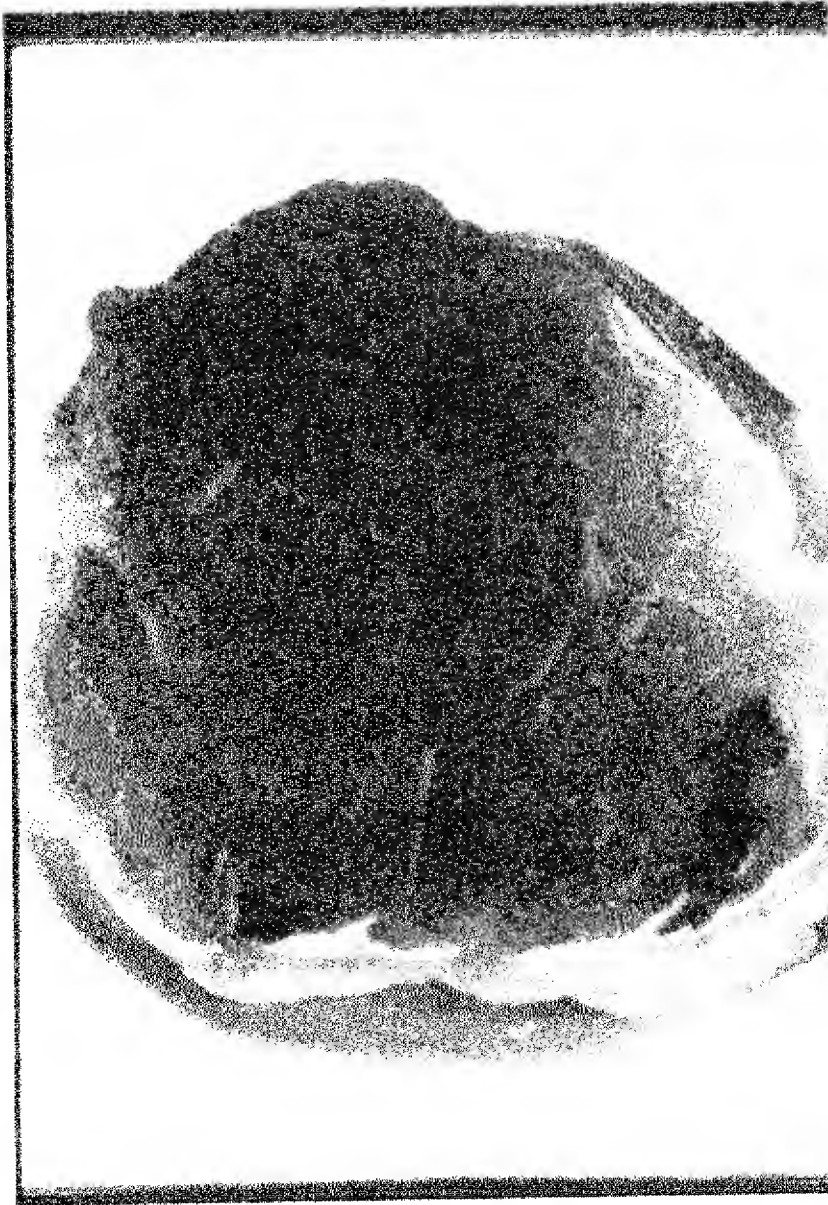
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Dissected Tooth Tissue Cysts - 7.5 Weeks



**Fig. 14**

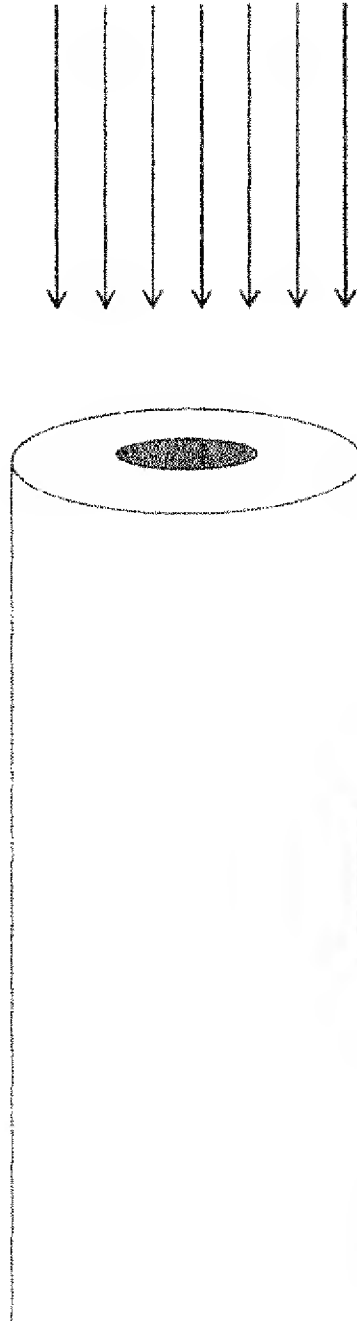
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**Tissue Samples Were Sectioned**



**Fig. 15**

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Goldner's Stain  
Green = mineralized tissue



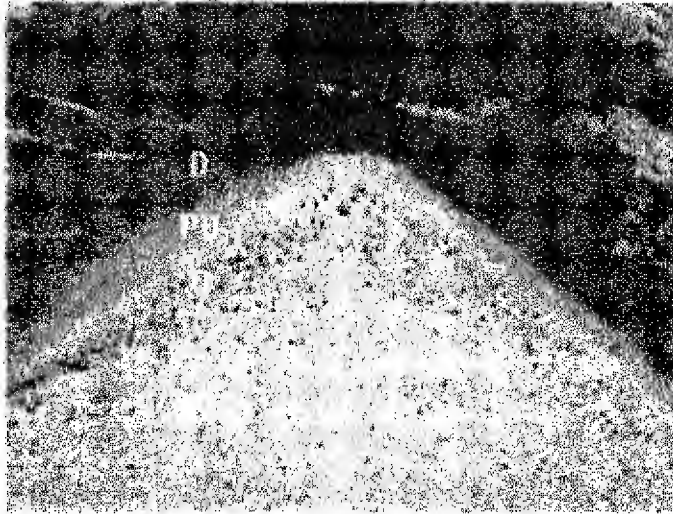
**Fig. 16**

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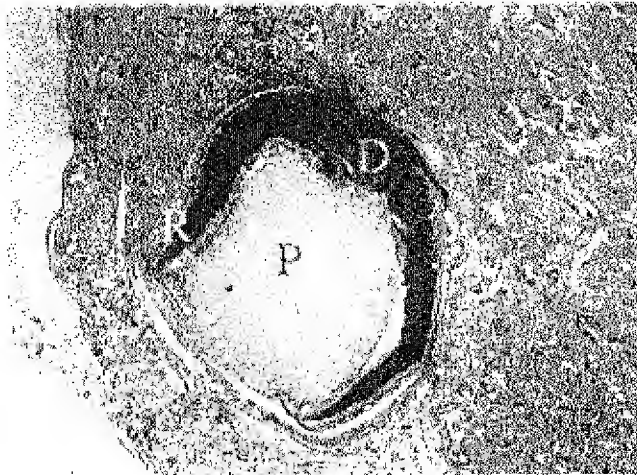
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**Fig. 17**

A



B

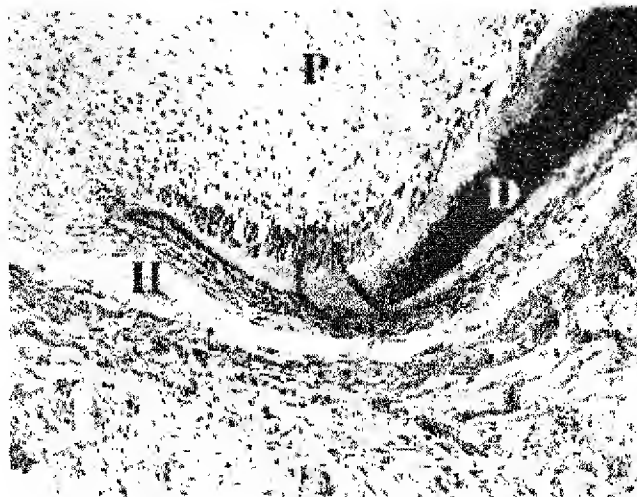


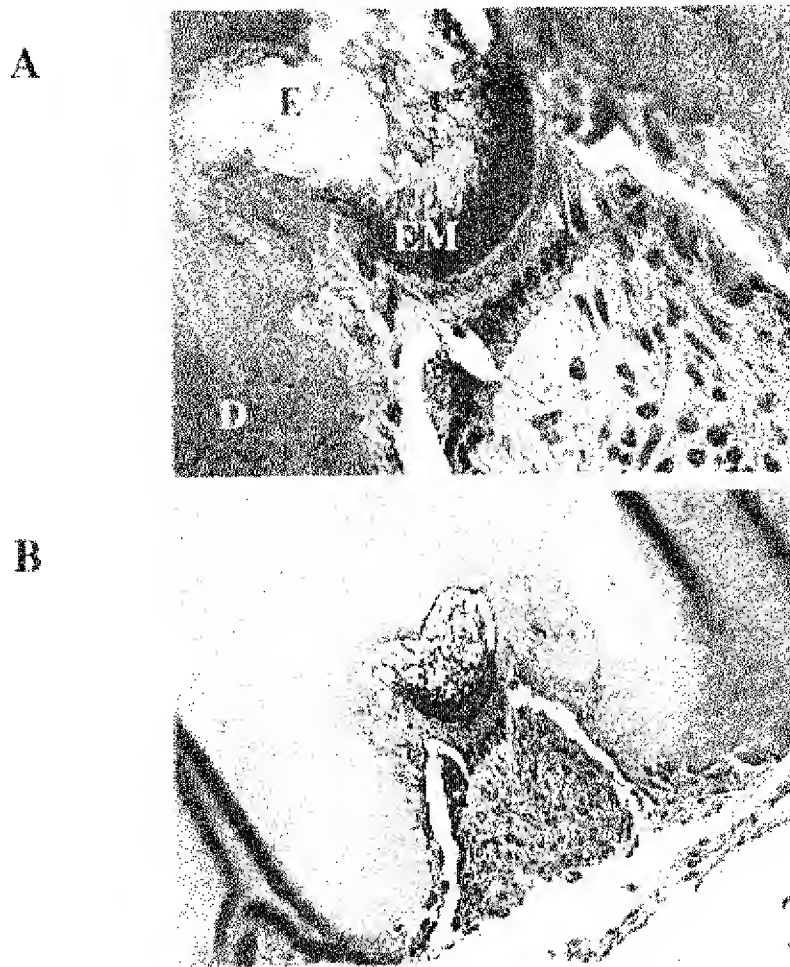
Fig. 18

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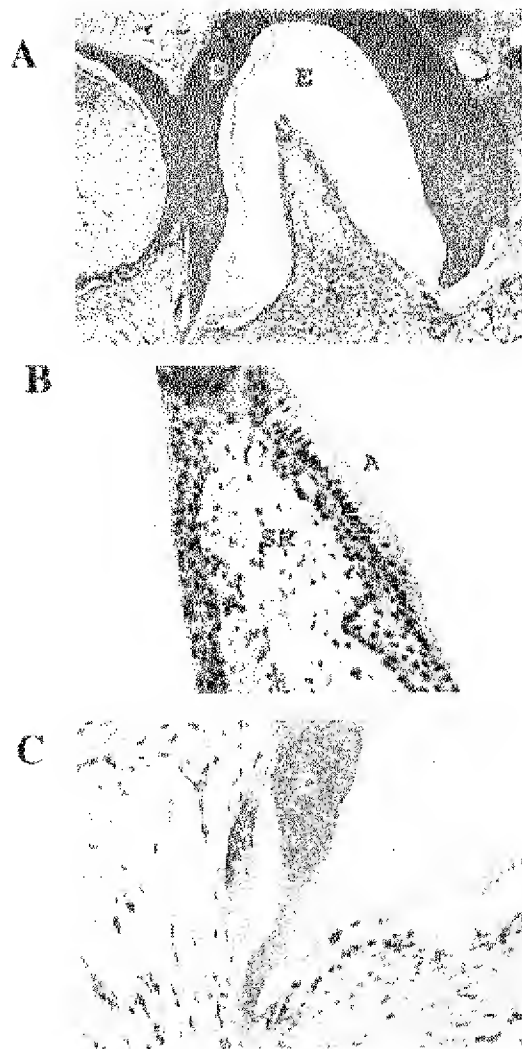
**Fig. 19**

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**Fig. 20**